REMARKS

Status of the claims

Claims 1-18 are pending in the application. Claims 7-9 and 16-18 are withdrawn from consideration. Claims 1-6 and 10-15 are rejected. No new matter is added herein.

35 U.S.C. §102(b) rejection

Claims 10-14 stand rejected under 35 U.S.C. §102(b) as being anticipated by **Chiesi** et al. (WO 00/06132A2) evidenced by **Basu** et al. (U.S. 2002/0025348A1) of record. This rejection is respectfully traversed.

The Examiner states on page 3 of the Office Action that **Chiesi** et al. teach that a pharmaceutical formulation for the treatment of inflammatory bowel disease containing as an active ingredient, beclomethasone dipropionate (BDP) and that the formulation demonstrates no systemic absorption of BDP and its major active metabolites. On page 3 of the Office Action, the Examiner cites **Basu** et al. which report that IBS (irritable bowel syndrome) also tends to occur in IBD (inflammatory bowel disease) patients who are in remission from their IBD symptomologies. As a result, the Examiner contends that claim 10 drawn to "a method of **alleviating the symptoms of irritable bowel syndrome in an individual in need of such treament**" (Examiner's emphasis) is anticipated by the prior art as evidenced by **Basu** et al. because **Basu** et al. report that IBS tends to occur in IBD patients who are in remission from their IBD symptmologies.

The Examiner goes on to state on pages 3 and 4 that IBD patients disclosed by **Chiesi et al. are the patients in need of treatment of irritable bowel syndrome** (Examiner's emphasis) because IBS tends to occur in IBD patients. Further, the mechanism of action of increasing the threshold of pain to colorectal distention, thereby alleviating the symptoms of irritable bowel syndrome in the individual would be inherent in **Chiesi's** method of treating inflammatory bowel disease comprising identical patients having IBD who are in need of alleviating the symptoms of irritable bowel syndrome as evidenced by **Basu** et al. Applicants respectfully disragree.

In order to anticipate a claim, each and every element of the claim should be described in a single prior art reference. Neither **Chiesi** et al. nor **Basu** et al. teach each and every element claimed in the instant invention. **Chiesi** et al. teach a pharmaceutical formulation for the treatment of inflammatory bowel disease (IBD) containing the active ingredient, beclomethasone dipropionate. There is however, no teaching of irritable bowel syndrome (IBS) in **Chiesi** et al.

The Examiner argues that this deficiency is overcome by **Basu** et al. which report that IBS also tends to occur in IBD patients who are in remission from their IBD symptomologies. The Applicants would like to respectfully point out that IBS and IBD have been regarded traditionally as separate disorders and despite some studies suggesting otherwise, any convergence of IBS and IBD is largely due to misdiagnosis (**Quigley**, Chin J Dig Dis. 2005; 6(3):122-132).

The Applicants submit Quigley, EM which states "In the past inflammatory bowel disease (IBD), celiac disease and irritable bowel syndrome (IBS) were regarded

as completely separate disorders. Now, with the description of inflammation, albeit low-grade, in IBS, and of symptom overlap between IBS and celiac disease, this contention has come under question. Is there true overlap between these disorders? Despite the limitations of available data one cannot but be struck by some areas of apparent convergence: IBD and celiac disease in remission, lymphocytic colitis and microscopic inflammation in IBS, in general, and, especially, in the post-infectious IBS category. The convergence between latent celiac disease and sub-clinical IBD, on the one hand, and IBS, on the other, appears, based on available evidence, to be somewhat spurious and may largely relate to misdiagnosis, a phenomenon which may also explain the apparent evolution of IBS into IBD in some studies." (abstract).

Applicants respectfully submit that a person having ordinary skill in this art would readily recognize that IBS and IBD are separate and unlinked disorders. For example, the NIH website states that "through the years, IBS has been called by many names, among them colitis, mucous colitis, spastic colon, or spastic bowel. However, no link has been established between IBS and inflammatory bowel diseases such as Crohn's disease or ulcerative colitis." (http://digestive.niddk.nih.gov/ddiseases/pubs/ibs/#what).

Furthermore, The Crohn's and Colitis Foundation of America (CCFA) website states that "Many people are confused about two distinct gastrointestinal disorders -- IBD and IBS. Different intestinal disorders can produce similar symptoms. Irritable bowel syndrome (IBS) is a condition that produces some symptoms similar to those of inflammatory bowel disease (IBD), but they are not the same condition, and they involve very different treatments. Therefore, getting an accurate diagnosis is

essential to managing your condition properly." (http://www.ccfa.org/about/news/ibsoribd). The website goes on to state that "IBS does not cause inflammation."

Furthermore, this distinction between IBS and IBD is inherent in and recognized by **Basu** et al. as claims 9 and 10 (U.S.2002/0025348) both depend on claim 7 for the treatment of bowel disorders. More specfically, claim 7 of **Basu** et al. recites a "method for treating a bowel disorder in a mammal, said method comprising identifying the mammal as suffering from a bowel disorder; administering the composition of matter of claim 1 or 2 to the mammal." In **Basu** et al., claim 9 further limits claim 7 for cases in which the bowel disorder is IBD whereas claim 10 further limits claim 7 for cases in which the bowel disorder is IBS. Obviously, if **Basu** et al. literally or inherently taught that IBS and IBD are identical forms of bowel disorders, **Basu** et al. would not be separately claimed IBD and IBS as claims 9 and 10 would have been duplicative and redundant with respect to one another. The Applicants submit, therefore, that claims 10-14 are not anticipated by **Chiesi** et al. further evidenced by **Basu** et al. Accordingly, the Applicants respectfully request the withdrawal of this rejection.

35 U.S.C. §103 rejection

Claims 1-6 and 15 stand rejected under 35 U.S.C. §103(a) as being unpatentable over **Chiesi** *et al* (WO 00/06132A2) in view of **Basu** et al (U.S.2002/0025348A1). Applicants respectfully traverse this rejection.

The teachings of **Chiesi** *et al* and **Basu** et al. cited by the Examiner are the same as discussed supra. The Examiner states that **Chiesi** *et al* do not teach the specified amounts of beclomethasone as set forth in claims 1-6 and 15. However, the Examiner states that it would have been obvious to one of ordinary skill in the art that the amount employed by **Chiesi** *et al* (3 mg or 5 mg) for the treatment of inflammatory bowel disease (irritable bowel syndrome related disorder) is within the recited amounts set forth in claims 1-6 and 15 because **Chiesi** *et al* in view of **Basu** et al. teach same individual having related disorder of irritable bowel syndrome comprising same effective dosages providing no systemic absorption of BDP as instantly claimed by the Applicant. Therefore, the Examiner states that **Chiesi** et al. obviously administered the same effective amounts within the Applicant's recited amount in order to have the same effect of treating inflammatory bowel disease which is related to irritable bowel syndrome. Additionally, the Examiner states that 5 mg amount employed by **Chiesi** *et al* is within the mg/kg recited in claims 1-6 and 15 when subject to be treated weighs 50 kg. For these reasons, the Examiner states that the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited reference. Hence, the Examiner rejects the claims for being obvious. Applicant respectfully disagrees.

Based on references of Quigley, EM, NIH website, and CCFA website discussed supra, it is very clear that IBS and IBD are distinct disorders. In fact, the prior art at the time the invention was filed and even today, teach that IBS and inflammatory bowel disease are distinct clinical syndromes in a variety of aspects including treatment (see Bradesi et al., 2003, previously made of record). As stated

supra, there is evidence in the relevant field that IBS and IBD are unlinked disorders and that IBS is not an inflammatory discorder as Basu et al. reports. IBD and IBS represent two conditions characterized by chronically recurring symptoms of abdominal pain, discomfort (urgency and bloating) and alterations in bowel habits. However, whereas IBD is characterized by inflammation or ulcerations in the small and/or large intestine, such "organic" changes have traditionally not been associated with IBS.

Although IBD is usually classified as ulcerative colitis or Crohn's disease, it also includes forms of microscopic colitis, e.g., histologic evidence of mucosal inflammation without macroscopic abnormalities. IBD is characterized by a constellation of patient-reported history and endoscopic, histopathologic and radiologic findings often with serologic correlates. Classic signs that reflect the inflammatory process within the gastrointestinal tract are rectal bleeding, diarrhea, fever and weight loss occasionally associated with extraintestinal manifestations. Interestingly, in the absence of complications, abdominal pain is not necessarily the most prominent symptom in inflammatory IBD despite extensive mucosal inflammation and presumably sensitization of peripheral visceral pain pathways. Genetic predisposition, environmental factors, infectious agents altered gut epithelial permeability and impaired immune responses have been incriminated in the still unclear cause of inflammatory bowel disease.

In contrast, IBS is classified as a functional bowel disorder and is currently diagnosed on the basis of a characteristic cluster of symptoms in the absence of detectable structural abnormalities. Indeed, according to the currently

used symptom criteria (Rome criteria), once organic changes are detected, a diagnosis of functional disorder can no longer be made. Due to the non-specificity of the cardinal symptoms of abdominal pain or abdominal discomfort, the current diagnosis of IBS applies to a heterogeneous group of patients, even after attempts to define subgroups based on predominant bowel habit. Current theories to explain the pathophysiology of IBS include alteration in the visceral perception, gastrointestinal motility and gut epithelia and immune function. Considerable evidence supports the role of psychosocial and physical stressors as central and peripheral triggers respectively of first symptom onset or exacerbation. Although there is a considerable interest in the putative role of low-grade chronic inflammation in the pathogenesis of IBS, enhanced responsiveness to psychosocial and physical stressors has been suggested as a plausible mechanism that could explain most clinical and experimental findings in IBS. Thus, there is ample evidence to show that IBS and inflammatory disease are distinct.

Chiesi et al. teach the use of topically active corticosteroid such as beclomethasone dipropionate in the treatment of inflammatory bowel diseases such as Ulcerative colitis and Crohn's disease. In this regard, **Chiesi** et al. disclose rectal or oral administration of beclomethasone dipropionate. There is no teaching or suggestion in **Chiesi** et al. that the administration of beclomethasone dipropionate is effective in treating irritable bowel syndrome. Additionally, **Basu** et al. does not cure this deficiency for the following reasons. First, the information in the art at the time of filing of the instant invention taught that IBS and inflammatory disorder are distinct. Second, there is a lack of histological evidence of inflammation in IBS. Additionally, there is evidence

that those skilled in the art generally believe these two disorders to be unlinked and that IBS is not inflammatory disorder. Thirdly, **Basu** et al. in fact teaches away from what the Examiner argues because as shown supra, **Basu** et al. teaches that they are in fact separate as recited in claims 9 and 10 (U.S.2002/0025348A1). Therefore, Applicants respectfully submit that claims 1-6 and 15 are not unpatentably obvious under 35 U.S.C. §103. Accordingly, Applicants respectfully request the withdrawal of the rejection claims 1-6 and 15 are not unpatentably obvious under 35 U.S.C. §103.

This is intended to be a complete response to the Office Action mailed June 3, 2008. Applicant encloses a Petition for Extension of time and Form PTO-2038 along with the response. In the absence of form PTO-2038, please charge applicable fees to Deposit Account 07-1185. If any issues remain outstanding, please telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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